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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/020,596	12/07/2001	Michael M. Becker	GP123-02.UT	6565

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EXAMINER	
CHAKRABARTI, ARUN K	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 05/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/020,596	Becker
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on *Apr 21, 2003* .

2a) [ ] This action is **FINAL**. 2b) [X] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) *1-60* is/are pending in the application.

4a) Of the above, claim(s) *37-60* is/are withdrawn from consideration.

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) *1-36* is/are rejected.

7) [ ] Claim(s) _____ is/are objected to.

8) [ ] Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) [ ] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on _____ is/are a) [ ] accepted or b) [ ] objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) [ ] All b) [ ] Some* c) [ ] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____ .
3. [ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) [ ] The translation of the foreign language provisional application has been received.

15) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) [X] Notice of References Cited (PTO-892)
2) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) [X] Information Disclosure Statement(s) (PTO-1449) Paper No(s). 1
4) [ ] Interview Summary (PTO-413) Paper No(s).
5) [ ] Notice of Informal Patent Application (PTO-152)
6) [X] Other: *Detailed Action*

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I, corresponding to claims 1-36, in Paper No. 0403 is acknowledged. The traversal is on the ground(s) that there is no burden to examine claims of Group II with claims of Group I and the classification is improper because kit claims of Group II comprises polycationic polymer in addition to nucleic acid probes. This is not found persuasive because in the presence of "comprising" language of the claims, any additional step(s) or materials can be included to separate the polycationic polymer from the nucleic acids. Moreover, examination of Group II claims will require not only the search of 10473 patents of Group I belonging to class 435, subclass 6, but also the search of 1885 patents of Group II belonging to class 536, subclass 22.1. This is prima facie burden of search, which has not been rebutted.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1, 3-5, 10, 11, 13-18, 28, 30, and 32-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Steeg et al. (U.S. Patent 5,753,437) (May 19, 1998).

Steeg et al teach a method for forming a duplex from polynucleotide probe and a target nucleic acid, the method comprising the steps of:

a) providing the probe to a test sample under conditions permitting the probe to preferentially hybridize to the target nucleic acid, if present, in the sample; and

b) providing a synthetic polycationic polymer (poly-lysine in this case) to the sample in an amount sufficient to inherently increase the association rate of the probe and the target nucleic acid in the sample under the conditions (Column 17, lines 54-67). This inherence is deduced from the fact that it was well known in the art at the time the invention was made (Mruyama et al. (1999), Nucleic Acids Symposium Series No. 42, pages 97-98; and Egholm et al. (U.S. Patent 6,297,016 B1) (October 2, 2001) (Column 14, lines 55-62)) that a synthetic polycationic polymer e.g., poly-lysine increases the stability and the association rate of the probe and the target nucleic acid.

Steeg et al teach a method, wherein the polymer is a graft copolymer having a delocalized charge (poly-lysine coated microscopic slides in this case) (Column 17, lines 55-60).

Steeg et al teach a method, wherein the probe is a polyanion (NM23 nucleic acid probe in this case) (Column 17, lines 61-63).

Steeg et al teach a method, wherein the probe further includes at least one of a cationic group and a nonionic group (nucleic acid probe attached to cationic polymer in this case) (Column 17, lines 55-60).

Steeg et al teach a method, wherein the target nucleic acid comprises ribosomal or messenger RNA (Column 14, line 2 to Column 17, line 66).

Steeg et al teach a method, wherein a complex comprising the polymer is formed in the sample under the conditions (Column 17, line 54 to Column 18, line 6).

Steeg et al inherently teach a method, wherein the complex includes a plurality of polymers which are covalently linked (Column 17, lines 55-60). This inherence is deduced from the fact that poly-lysine comprises lysine molecules covalently attached together.

Steeg et al inherently teach a method, wherein the complex includes polymers and polynucleotides which are covalently linked (Column 17, lines 55-60).

Steeg et al teach a method further comprising providing to the sample a dissociating reagent to dissociate the polymer from the probe and the target nucleic acid (Column 17, lines 55-60).

Steeg et al teach a method, wherein the conditions include a temperature of at least about 40 degree centigrade (37 degree centigrade to be precise) and an 5-150 mM equivalent salt concentration containing multivalent cations (Column 17, lines 55-67).

Steeg et al teach a method, wherein the polymer is provided to the sample before the probe (Column 17, lines 54-60).

Steeg et al teach a method further comprising determining whether the duplex has formed in the sample (Column 17, line 67 to Column 18, line 6).

Steeg et al teach a method, wherein the probe preferentially hybridizes to a target nucleic acid sequence contained in the target nucleic acid under the conditions and the determining step is diagnostic for the presence or absence of a virus or organism or members of a group of viruses or organisms in the sample (Column 18, line 30 to column 19, line 16).

Steeg et al teach a method, wherein the probe stably hybridizes to one or more nucleic acid sequences present in the sample having at least a single base difference from the target nucleic acid sequence (Column 9, lines 16-30).

Steeg et al teach a method, wherein the probe includes a label (Column 17, lines 60-63).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 2, 6, 7, 12, 21-25, 29, and 31 are rejected under 35 U.S.C. 103(a) over Steeg et al. (U.S. Patent 5,753,437) (May 19, 1998).

Steeg et al teach the method of claims 1, 3-5, 10, 11, 13-18, 28, 30, and 32-36 as described above.

Steeg et al do not teach the method, wherein a) the cationic monomers comprising the polymer are in excess of the phosphate groups of the probe, b) the concentration of the polymer in the sample is in the range of about 10 micromolar to about 100 micromolar, c) the polymer has a weight average molecular weight of less than about 300,000 Da, d) the distance between adjacent cationic monomers of the polymer approximates the distance between adjacent phosphate groups of the probe and the target nucleic acid, e) the temperature is up to about 60 degree centigrade, and f) the association rate of the probe and the target nucleic acid under the conditions and in the presence of the polymer is 2-1000 fold greater than the association rate of the probe and the target nucleic acid under the conditions and in the absence of the polymer.

However, it is *prima facie* obvious that selections of a) the specific concentration of the cationic monomers and b) the polymer, c) the specific average molecular weight of the polymer, d) the specific distance between adjacent cationic monomers of the polymer, e) the specific temperature of hybridization and f) the specific association rate between the probe and the target nucleic acid, represent routine optimization of the polymer with regard to the length and structure of the unknown portion of the target nucleic acid and the probe under study which routine optimization parameters are explicitly recognized to an ordinary practitioner in the relevant art. As noted *In re Aller*, 105 USPQ 233 at 235,

> More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Routine optimization is not considered inventive and no evidence has been presented that a) the specific concentration of the cationic monomers and b) the polymer, c) the specific average molecular weight of the polymer, d) the specific distance between adjacent cationic monomers of the polymer, e) the specific temperature of hybridization, selection performed was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

6. Claims 8, and 9 are rejected under 35 U.S.C. 103(a) over Steeg et al. (U.S. Patent 5,753,437) (May 19, 1998) in view of Lee et al. (U.S.Patent 6,448,407 B1) (September 10, 2002)

Steeg et al teach the method of claims of claims 1-7, 10-18, and 28-36 as described above.

Steeg et al do not teach the method, wherein the probe includes multiple interacting labels and comprises first and second base regions which hybridizes to each other under the conditions in the absence of the target nucleic acid, wherein the labels interact with each other to produce a first detectable signal when the probe is not hybridized to the target nucleic acid and a second detectable signal when the probe is hybridized to the target nucleic acid, and wherein the first and second signals are detectably different from each other.

Lee et al. teach the method, wherein the probe includes multiple interacting labels and comprises first and second base regions which hybridizes to each other under the conditions in the absence of the target nucleic acid, wherein the labels interact with each other to produce a first detectable signal when the probe is not hybridized to the target nucleic acid and a second

detectable signal when the probe is hybridized to the target nucleic acid, and wherein the first and second signals are detectably different from each other (Column 27, lines 28-47).

Steeg et al do not teach the method, wherein the probe includes a third base region which hybridizes to the target nucleic acid under the conditions, and wherein the third base region is distinct from the first and second base regions or the third base region partially or fully overlaps at least one of the first and second base regions of the probe.

Lee et al. teach the method, wherein the probe includes a third base region which hybridizes to the target nucleic acid under the conditions, and wherein the third base region is distinct from the first and second base regions or the third base region partially or fully overlaps at least one of the first and second base regions of the probe (Column 27, lines 28-47).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute a method, wherein the probe includes multiple interacting labels and comprises first and second base regions which hybridizes to each other under the conditions in the absence of the target nucleic acid, wherein the labels interact with each other to produce a first detectable signal when the probe is not hybridized to the target nucleic acid and a second detectable signal when the probe is hybridized to the target nucleic acid, and wherein the first and second signals are detectably different from each other of Lee et al in the method of Steeg et al. since Lee et al. states, "Hybridization probes labelled with different fluorescent dyes, including the atropisomeric dyes of the invention, enable multiplex, homogeneous hybridization assays to be carried out in sealed reaction tubes (Column 27, lines 44-

47). " By employing scientific reasoning, an ordinary artisan would have combined and substituted a method,wherein the probe includes multiple interacting labels and comprises first and second base regions which hybridizes to each other under the conditions in the absence of the target nucleic acid, wherein the labels interact with each other to produce a first detectable signal when the probe is not hybridized to the target nucleic acid and a second detectable signal when the probe is hybridized to the target nucleic acid, and wherein the first and second signals are detectably different from each other of Lee et al in the method of Steeg et al. in order to improve the analysis of a plurality of target nucleic acid. An ordinary practitioner would have been motivated to combine and substitute a method,wherein the probe includes multiple interacting labels and comprises first and second base regions which hybridizes to each other under the conditions in the absence of the target nucleic acid, wherein the labels interact with each other to produce a first detectable signal when the probe is not hybridized to the target nucleic acid and a second detectable signal when the probe is hybridized to the target nucleic acid, and wherein the first and second signals are detectably different from each other of Lee et al in the method of Steeg et al., in order to achieve the express advantages, as noted by Lee et al., of a novel invention that enables multiplex, homogeneous hybridization assays to be carried out in sealed reaction tubes.

7. Claim 19 is rejected under 35 U.S.C. 103(a) over Steeg et al. (U.S. Patent 5,753,437) (May 19, 1998) in view of Egholm et al. (U.S. Patent 6,297,016 B1) (October 2, 2000).

Steeg et al teach the method of claims of claims 1-7, 10-18, and 28-36 as described above.

Steeg et al do not teach the method, wherein the complex is water soluble.

Egholm et al. teach the method, wherein the complex is water soluble (Column 14, line 55 to Column 15, line 6, and Example 4).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute a method, wherein the complex is water soluble of Egholm et al in the method of Steeg et al. since Egholm et al. states, "Hybridization-stabilizing moieties may increase the stability of base-pairing, i.e., the affinity, or the rate of hybridization, exemplified by high thermal melting temperatures, Tm, of the duplex. Hybridization-stabilizing moieties may also increase the specificity of base-pairing (Column 14, lines 55-64). " An ordinary practitioner would have been motivated to combine and substitute a method, wherein the complex is water soluble of Egholm et al in the method of Steeg et al., in order to achieve the express advantages, as noted by Egholm et al., of a novel invention that provides hybridization-stabilizing moieties that may increase the stability of base-pairing, i.e., the affinity, or the rate of hybridization and may also increase the specificity of base-pairing.

8. Claims 26-27 are rejected under 35 U.S.C. 103(a) over Steeg et al. (U.S. Patent 5,753,437) (May 19, 1998) in view of Horn et al. (U.S.Patent 6,465,175 B2) (October 15, 2002).

Steeg et al teach the method of claims of claims 1-7, 10-18, and 28-36 as described above.

Steeg et al do not teach the method, further comprising providing to the sample a dissociating reagent (a polyanion or an anionic detergent) to dissociate the polymer from the probe and the target nucleic acid.

Horn et al. teach the method, further comprising providing to the sample a dissociating reagent (a polyanion or an anionic detergent) to dissociate the polymer (a label in this case) from the probe and the target nucleic acid (Column 9, lines 57-61).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute a method comprising providing to the sample a dissociating reagent (a polyanion or an anionic detergent) to dissociate the polymer from the probe and the target nucleic acid. of Horn et al in the method of Stegg et al. since Horn et al. states, "Another primary focus of the invention is to provide a signal amplification system that produces a greater yield of detectable signal than possible with previous systems (Column 9, lines 64-67). " An ordinary practitioner would have been motivated to combine and substitute a method comprising providing to the sample a dissociating reagent (a polyanion or an anionic detergent) to dissociate the polymer from the probe and the target nucleic acid. of Horn et al in the method of Stegg et al., in order to achieve the express advantages, as noted by Horn et al., of a novel invention that provides a signal amplification system that produces a greater yield of detectable signal than possible with previous systems.

Conclusion

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph. D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119. The fax phone number for this Group is (703)746-4979.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237.

Arun kr. Chakrabarti

ARUN K. CHAKRABARTI
PATENT EXAMINER

Arun Chakrabarti,

Patent Examiner,

April 30, 2003